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(54) Title: BIOLOGICALLY ACTIVE COMPLEX COMPRISING ALPHA-LCATABUMIN OR A VARIANT THEREOF, AND A COFACTOR

(57) Abstract: A biologically active complex comprising alpha-lactalbumin or a variant of alpha-lactalbumin which is in the apo folding state, or a fragment of either of any of these, and a cofactor which stabilizes the complex in a biologically active form, provided that any fragment of alpha-lactalbumin or a variant thereof comprises a region corresponding to the region of α -lactalbumin which forms the interface between the alpha and beta domains, and further provided that when the complex comprises native alpha-lactalbumin, the cofactor is other than C18:1:9 cis fatty acid. These complexes have therapeutic applications for example in the treatment of cancer and as antibacterial agents.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 01293

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/76 A61K38/38 A61K47/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, WPI Data, CHEM ABS Data, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | <p>WO 99 26979 A (HAAKANSSON PER ANDERS ;SVENSSON MALIN WILHELMINA (SE); SVANBORG CA) 3 June 1999 (1999-06-03) page 1, line 11 - line 14 page 1, line 21 - line 33 page 3, line 15 - line 26 page 4, line 1 - line 4 page 5, line 8 - line 24 page 6, line 19 - line 26 page 7, line 30 -page 8, line 5; example 10</p> <p style="text-align: center;">--- -/--</p> | 1-14 |

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 01293

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| X | <p>M. SVENSSON ET AL: "Conversion of alpha-lactalbumin to a protein inducing apoptosis" PNAS, vol. 97, no. 8, 11 April 2000 (2000-04-11), pages 4221-4226, XP002250705 see especially page 4225, right column, paragraph six</p> | 1-14 |
| X | <p>ANDERS HÅKANSSON ET AL: "A folding variant of alpha-lactalbumin with bactericidal activity against Streptococcus pneumoniae" MOLECULAR MICROBIOLOGY, vol. 35, no. 3, 2000, pages 589-600, XP002250706 the whole document</p> | 1-14 |
| A | <p>DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; October 2001 (2001-10) PERMYAKOV SERGEI E ET AL: "Mutating aspartate in the calcium-binding site of alpha-lactalbumin: Effects on the protein stability and cation binding." Database accession no. PREV200200099182 XP002250707 abstract & PROTEIN ENGINEERING, vol. 14, no. 10, October 2001 (2001-10), pages 785-789, ISSN: 0269-2139</p> | 4-6 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 03/01293

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: **13-14**
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210

2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 13-14

Claims 13-14 relate to methods of treatment of the human or animal body by surgery or by therapy/diagnostic methods practised on the human or animal body/Rule 39.1.(iv). Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the compounds/compositions.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB/01293

| Patent document cited in search report | | Publication date | | Patent family member(s) | | Publication date |
|--|---|------------------|----|-------------------------|--|------------------|
| WO 9926979 | A | 03-06-1999 | AU | 1254199 A | | 15-06-1999 |
| | | | EP | 1032596 A1 | | 06-09-2000 |
| | | | WO | 9926979 A1 | | 03-06-1999 |
| | | | JP | 2001524491 T | | 04-12-2001 |
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